UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,858	03/02/2005	Hiroyoshi Hidaka	8279.829USWO	5428

7590 07/18/2007

Hamre Schumann Mueller & Larson P. C.
P.O. BOX
Minneapolis, MN 55402

EXAMINER
GEMBEH, SHIRLEY V

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
07/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,858	HIDAKA ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,16 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,16 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Action

Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

The response filed **6/12/07** presents remarks and arguments to the office action mailed **1/12/07**. Applicants' request for reconsideration of the rejection of claims in the last office action has been considered.

Applicants' arguments, filed, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of Claims

Claims 15-16 and 27 are pending and examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15-16 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating leukemia, does not reasonably provide enablement for the wide variation of malignant tumors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2nd 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

Nature of the invention state of the prior art, relative skill of those in the art and the predictability of the art.

The nature of the invention is to a method of treating a patient suffering from malignant tumor comprising administering therapeutically effective amount of the compoundof formula I in combination with at least one of cisplatin and carboplatin. As

stated, however, claims 15-16 and 27 recite that any or a very large representation of malignant tumor disease are intended with the compound of claim 27 and its large representation of the substituent groups. For example malignant tumors of colon and rectum which include adenocarcinoma, lymphoma, leiomyosarcoma etc (see Types of colon cancer as evident by Donna Myers enclosed). Next, the compound has a wide variation of substituents, these substituents all do not carry the same activity. As evident by Kern et al., structural activity relationship varies, while some gave positive result on the treatment of human melanoma some showed no activity (see for example Table I , pg, 5180). The nature of the invention is very broad, and the relative skill of those in the art is generally that of a Ph.D. or M.D. with expertise in the field of malignant tumor diseases. Each particular malignant tumor disease has its own specific characteristics and etiology. The unpredictability observed with single agent therapy is compounded when a combination of agents is employed. The broad recitation "treating a malignant tumor disease" is inclusive of many conditions that presently have no established successful therapies.

It is clear the art to which the present invention relates is highly unpredictable and unreliable with respect to conclusions drawn from laboratory data extrapolated to clinical efficacy.

<u>The breadth of the claims</u>

The claims are very broad and inclusive of a wide representation of malignant tumors

<u>The amount of direction or guidance provided and the presence or absence of</u>

working examples

The example given ids for the treatment of leukemis (see page 20) in a mice and no indication of how to extrapolate the data for the treatment of wide variation of malignant tumors in a patient.

The quantity of experimentation necessary

Presently, guidance as to which particular malignant tumor is contemplated according to the recited limitations in the claims is absent. In particular, with respect to methods of treating malignant tumor, the skilled artisan would expect the interaction of a particular combination of drugs in the treatment of a particular disease state to be very specific and highly unpredictable absent a clear understanding of the structural and biochemical basis for each agent. Absent reasonable a priori expectations of success for using the particular combination of compound of formula I with a representation of atleast one therapeutic agent one skilled in the art of malignant tumors would have to test extensively many disease states to discover which show efficacy. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do otherwise.

Maintained Claim Rejections - 35 USC § 103

Claims 15-16 and 27 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Hidaka et al., US 5,972,976 in view of Goodman and Gilman, The Pharmacological

Basis of therapeutics,and Ragaz et al., The new England J. of Med. (As in the office action of record).

Applicant again argues that synergism is taught in the Table 1 of the specification that Table 1, results are shown where compound 2 is administered alone at a maximum tolerated dose of 100 mg/kg, and where CDDP is administered alone at a maximum tolerated dose of 10 mg/kg. When compound 2 is administered alone at a maximum tolerated dose of 100 mg/kg, the maximum T/C % is 165% or 150%. When CDDP is administered alone at a maximum tolerated dose of 10 mg/kg, the maximum T/C % is 170%. In both instances of single administration, no survival is observed.

In response the results still does not show synergism. Synergism is the interaction of two or more agents so that their combined effect is greater than the sum of their individual effects. (165 + 170 = 335) The results are merely additive. If Applicant is basting the survival rate on the unexpected result then it can be considered.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SVG
7/10/07

BRIAN-YONG S. KWON
PRIMARY EXAMINER